

REMARKS

As an initial matter, Applicants wish to thank the Examiner for the courtesy of an interview on September 13, 2004. At the interview the Applicants' representative discussed all of the rejections of record. The instant amendments and response reflect the substance of the interview.

I. Amendments to the Specification and Claims

Applicants first amend the specification to remove the incorporation by reference from the priority application information. Claims 85-89, 91, 95-96, 98, 99, 101, 102, and 104-121 are pending and under examination. Applicants thank Examiner Woitach for withdrawing the previous restriction and election requirements, the rejections under §112, and objections to the specification and Oath/Declaration.

Applicants amend claim 85 to recite that electrically stimulating said at least one striated muscle cell with at least one unipolar pulse of an electric field intensity ranging from 1 to 800 V/cm and wherein said electric stimulation is greater than 10 milliseconds in duration. Support for this amendment can be found, for example, on page 6, lines 18-21 of the instant specification. Support for new claim 121 can also be found in this passage. Applicants respectfully request entry of these amendments.

II. Priority

The Office states that while the claim for priority to US provisional application 60/067,488, filed December 1, 1997, and French application 97/08233 filed June 30, 1997, has been made in the first line of the specification, because of the filing date of

the instant application and the date where the specification was amended to indicate the claim for priority, the appropriate petition must be filed to recognize this priority. As a result the office indicated that the priority date given the instant application was June 30, 1998, the date of filing of the PCT application.

However, as agreed by the Examiner at the interview, Applicants are entitled to the priority dates of the US provisional and the French application. M.P.E.P § 201.11 states "If an applicant includes a claim to the benefit of a prior application elsewhere in the application but not the manner specified in 37 CFR 1.78(a)(2)(i) and (a)(2)(iii) or 37 CFR 1.78(a)(5)(i) and (a)(5)(iii) (e.g., if the benefit claim is included in an unexecuted oath or declaration or the application transmittal letter) within the time period set forth in 37 CFR 1.78(a)(2)(ii) or (a)(5)(ii), the Office will not require a petition and the surcharge under 37 CFR 1.17(t) to correct the benefit claim if the information concerning the benefit claim contained elsewhere in the application was recognized by the Office as shown by its inclusion on a filing receipt." M.P.E.P § 201.11. As evidenced by the Official Filing Receipt mailed on July 17, 2002, the Office has recognized the benefit claim in question. Therefore, no petition is required in order to correct the benefit claim information and Applicants respectfully request that the Examiner acknowledge priority of the instant application to US provisional application 60/067,488, filed December 1, 1997, and French application 97/08233 filed June 30, 1997.

The Examiner objected to the recitation of "are incorporated by reference herein" in the priority claim as adding new matter. Applicants respectfully traverse but in order to advance prosecution have removed this statement from the specification.

III. Information Disclosure Statement

The Office objects to the Information Disclosure Statement (IDS) filed March 24, 2004 as failing to comply with 37 CFR 1.97(c) because it lacks a statement as specified in 37 CFR 1.97(e). (Office Action at page 4.) However, an Information Disclosure Statement filed under 37 CFR 1.97(c) does not require a statement as specified in 37 CFR 1.97(e).

The IDS filed on March 24, 2004 was filed after the period specified in §1.97(b) but before the mailing date of any of a final action under §1.113, a notice of allowance under §1.311, or an action that otherwise closes prosecution in the application. Thus, according to §1.97(c), the IDS must be accompanied by **one** of: (1) The statement specified in §1.97(e) **OR** (2) The fee set forth in §1.17(p). The IDS filed on March 24, 2004 included the fee as specified in §1.17(p), therefore the statement under §1.97(e) was not required. Applicants request that this objection be withdrawn.

IV. Rejections under 35 U.S.C. § 102

The Office rejects claims 85, 91, 98, 99, 100, 102, 104-106, 111 and 118-120 under 35 U.S.C. § 102(a) or § 102(e), as allegedly anticipated by one or more of Dev et al. (WO 96/39226; "Dev I"), Dev et al. (U.S. Patent No. 5,993,434; "Dev II"). Applicants respectfully traverse each of these rejections.

As discussed at the interview, in order to advance prosecution, Applicants have amended claim 85 to recite "wherein said electric stimulation is greater than 10 milliseconds in duration." At the interview the Examiner indicated that the combination of contacting *in vivo* at least one striated muscle cell with at least one nucleic acid, and

electrically stimulating said at least one striated muscle cell with at least one unipolar pulse of an electric field intensity ranging from 1 to 800 V/cm and wherein said electric stimulation is greater than 10 milliseconds in duration, distinguishes over the prior art of Dev et al.

A *prima facie* case of anticipation requires that a single publication teaches, either expressly or inherently, each and every element or limitation of the claim, including any functional limitations. M.P.E.P. § 2131. Moreover, as discussed at the interview, Dev I and II provide a broad generic description of electroporation mediated delivery of drugs and genes, analogous to a genus, and there is no specific teaching of the claimed invention. Even assuming that the claimed invention is a species within the genus of methods for electroporation described by the Dev references, for there to be anticipation, one must “at once envisage” the claimed species based on the teaching of the prior art genus. *Ex parte A*, 17 USPQ2d 1716 (Bd Pat. App. & Inter. 1990). The Dev references only provide a laundry list of possible conditions for electroporation and possible in vivo targets but never provide any direction to reach the combination of the claimed invention. As the Examiner agreed at the interview, one does not at once envisage the claimed combination as amended and the Applicants respectfully request that this rejection be withdrawn.

V. Rejections under 35 U.S.C. § 103

Claims 85-89, 91, 95, 96, 98-102, 104-117 and 118-120 were rejected under 35 U.S.C. § 103 as being unpatentable over Dev I and Dev II, “Wolff I” (U.S. Patent No. 5,693,622) and “Wolff II” (U.S. Patent No. 6,228,844). (Office Action at pages 11-14.) Applicants respectfully disagree.

As described above, and as agreed by the Examiner at the interview, the Dev and Wolf references do not teach or suggest the combined combination as amended. In order for the Office to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. See M.P.E.P. ' 2143. Importantly, this evidence of a teaching, suggestion, or motivation to combine must be "clear and particular." *In re Dembiczak*, 175 F.3d 994 (Fed Cir. 1999). One cannot pick and choose only those elements of a reference that support a rejection while omitting other elements that do not support the rejection. *In re Wesslau*, 147 U.S.P.Q. 391, 393 (C.C.P.A. 1965).

The Dev references provide a laundry list of possible conditions for electroporation and possible in vivo targets, but the reference leads the skilled artisan to electrotransfer into tumor cell lines at a field strength of 1,000 or 1,300 V/cm. (See Dev II at columns 11 and 12 and Figure 12b.) Dev also teaches pulses of 99 microseconds. (Dev I at page 17, line 13, and page 18, line 19.) In contrast, Applicants' claims, as amended, are directed to an electric field intensity ranging from 1 to 800 V/cm and recite a duration of "greater than 10 milliseconds." Thus Dev does not provide motivation to achieve the claimed combination.

Moreover, as described in the response of March 23, 2004, The duration of the pulse, like the electric field intensity, is not a simple variable. Instead, Applicants' working examples show that the pulse duration may have a significant effect on the uptake of nucleic acids into striated muscle cells as well as on the safety of the transfection procedure.

Applicants working examples illustrate that one of ordinary skill in the art following Dev's suggestions to use intensities of 1,000 or 1,300 V/cm would not successfully obtain the claimed invention. For instance, Example 1 uses the prior art electroporation conditions of 800 to 1,200 V/cm in order to introduce luciferase DNA into the striated muscle cells in the legs of mice. (Application at pages 30-33 and Figures 1A and 1B.) Surprisingly, pulses of 800 to 1,200 V/cm actually yielded lower signals of luciferase than the controls in which the DNA was simply injected. (Id. at page 32, and Figures 1A and 1B.) Moreover, these high field intensities also damaged the muscle tissue. (Application at page 33, lines 3-5.) In fact, these results as a whole support the teachings of Wolff to simply inject DNA into muscle tissue and allow the cells to take it up unaided.

Applicants' surprisingly discovered, however, that longer pulses of lower intensity, such as 100, 200, or 400 V/cm, are safe to the muscle tissue and can increase the luciferase intensity in the tissue over simple injection by 200-fold. (Application at pages 33-36, and Figures 2-4.) This data is also summarized in a paper by the instant inventors, which is submitted herewith. (L.M. Mir et al., *Sciences de la Vie/Life Sciences* 321: 893-899 (1998).)

Thus, Applicants' data also show unexpected results. Such unexpected results alone can be sufficient for patentability, even when a claimed invention would otherwise have been found obvious. M.P.E.P. § 2144.09.

For all of these reasons, the combination of Dev I, Dev II, Wolff I, and Wolff II does not establish a *prima facie* case of obviousness, while Applicants' invention also

shows unexpected results. Thus, Applicants respectfully request the withdrawal of this rejection.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any required fees not found herewith to Deposit Account No. 06-0916.

Respectfully submitted,

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